Amendments to the Specification

Please amend the paragraph at page 14, line 22, continuing through page 15, line 5, to read as follows:

The stabilized pharmaceutical formulations of the invention comprise IFN-β and variants thereof. The term "IFN-β" as used herein refers to IFN-β or variants thereof, sometimes referred to as IFN-β-like polypeptides. Human IFN-β variants, which may be naturally occurring (e.g., allelic variants that occur at the IFN-β locus) or recombinantly produced, have amino acid sequences that are the same as, similar to, or substantially similar to the mature native IFN-β sequence shown in SEQ ID NO:1. Fragments of IFN-β or truncated forms of IFN-β that retain their activity are also encompassed. These biologically active fragments or truncated forms of IFN-β are generated by removing amino acid residues from the full-length IFN-β amino acid sequence using recombinant DNA techniques well known in the art. IFN-β polypeptides may be glycosylated or unglycosylated, as it has been reported in the literature that both the glycosylated and unglycosylated IFN-β's show qualitatively similar specific activities and that, therefore, the glycosyl moieties are not involved in and do not contribute to the biological activity of IFN-β.

Please amend the paragraph at page 15, lines 6-21, to read as follows:

The IFN-β variants encompassed herein include muteins of the mature native IFN-β sequence shown in SEQ ID NO:1, wherein one or more cysteine residues that are not essential to biological activity have been deliberately deleted or replaced with other amino acids to eliminate sites for either intermolecular crosslinking or incorrect intramolecular disulfide bond formation. IFN-β variants of this type include those containing a glycine, valine, alanine, leucine, isoleucine, tyrosine, phenylalanine, histidine, tryptophan, serine, threonine, or methionine substituted for the cysteine found at amino acid 17 of the mature native amino acid sequence. Serine and threonine are the more preferred replacements because of their chemical analogy to cysteine. Serine substitutions are most preferred. In one embodiment shown in SEQ ID NO:2,

the cysteine found at amino acid 17 of the mature native sequence shown in SEQ ID NO:1 is replaced with serine. Cysteine 17 may also be deleted using methods known in the art (see, for example, U.S. Patent No. 4,588,584, herein incorporated by reference), resulting in a mature IFN-β mutein that is one amino acid shorter than the mature native IFN-β. See also, as examples, U.S. Patent Nos. 4,530,787; 4,572,798; and 4,588,585. Thus, IFN-β variants with one or more mutations that improve, for example, their pharmaceutical utility are also encompassed by the present invention.

Please amend the paragraph at page 17, line 12, continuing through page 18, line 5, to read as follows:

Thus, the determination of percent identity between any two sequences can be accomplished using a mathematical algorithm. One preferred, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller (1988) *Comput. Appl. Biosci.* 4:11-7. Such an algorithm is utilized in the ALIGN program (version 2.0), which is part of the GCG alignment software package. A PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used with the ALIGN program when comparing amino acid sequences. Another preferred, non-limiting example of a mathematical algorithm for use in comparing two sequences is the algorithm of Karlin and Altschul (1990) *Proc. Natl. Acad. Sci. USA* 90:5873-5877, modified as in Karlin and Altschul (1993) *Proc. Natl. Acad. Sci USA* 90:5873-5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul *et al.* (1990) *J. Mol. Biol.* 215:403-410. BLAST amino acid sequence searches can be performed with the XBLAST program, score = 50, wordlength = 3, to obtain amino acid sequence similar to the polypeptide of interest. To obtain gapped alignments for comparison purposes, gapped BLAST can be utilized as described in Altschul *et al.* (1997) *Nucleic Acids Res.* 25:3389-3402. Alternatively, PSI-BLAST can be used to perform an integrated search that detects distant relationships between molecules. See Altschul *et al.* (1997) *supra*. When utilizing BLAST, gapped BLAST, or PSI-BLAST programs, the default parameters can be used. *See* ~~http://www.ncbi.nlm.nih.gov~~ www.ncbi.nlm.nih.gov.

Also see the ALIGN program (Dayhoff (1978) in *Atlas of Protein Sequence and Structure* 5:Suppl. 3, National Biomedical Research Foundation, Washington, D.C.) and programs in the Wisconsin Sequence Analysis Package, Version 8 (available from Genetics Computer Group, Madison, Wisconsin), for example, the GAP program, where default parameters of the programs are utilized.

Please amend the paragraph at page 18, line 23, continuing through page 19, line 6, to read as follows:

Biologically active variants of IFN-β encompassed by the invention should retain IFN-β activities, particularly the ability to bind to IFN-β receptors. In some embodiments, the IFN-β variant retains at least about 25%, about 50%, about 75%, about 85%, about 90%, about 95%, about 98%, about 99% or more of the ~~biologically~~biological activity of the polypeptides whose amino acid sequences are given in ~~Figure 1 or 2~~SEQ ID NO:1 or 2. IFN-β variants whose activity is increased in comparison with the activity of the polypeptides shown in ~~Figure 1 or 2~~ SEQ ID NO:1 or 2 are also encompassed. The biological activity of IFN-β variants can be measured by any method known in the art. Examples of such assays can be found in Fellous *et al.* (1982) *Proc. Natl. Acad. Sci USA* 79:3082-3086; Czerniecki *et al.* (1984) *J. Virol.* 49(2):490-496; Mark *et al.* (1984) *Proc. Natl Acad. Sci. USA* 81:5662-5666; Branca *et al.* (1981) *Nature* 277:221-223; Williams *et al.* (1979) *Nature* 282:582-586; Herberman *et al.* (1979) *Nature* 277:221-223; Anderson *et al.* (1982) *J. Biol. Chem.* 257(19):11301-11304; and the IFN-β potency assay described herein (see Example 2).